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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/915,931	07/26/2001	Hilton A. Salhanick	62694-A/JPW/SHS	8253

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EXAMINER	
DAVIS, DEBORAH A	

ART UNIT	PAPER NUMBER
1641	14

DATE MAILED: 02/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/915,931	SALHANICK ET AL.	
	Examiner	Art Unit	
	Deborah A Davis	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *94-101,110-122 and 132-134* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *94-101,110-122 and 132-134* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response to the Office Action mailed November 13, 2003 is acknowledged. Currently, claims 94-101, 110-122 and 132-134 are pending and under examination.

2. In the previous Office Action (Paper #12) Examiner inadvertently indicated that claims 132-134 were withdrawn from consideration. However, to make the record clear, these claims are currently pending and under examination.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 94-101 and 132-133 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harsoulis et al (Journal of endocrinology, 1974, Vol. 62, pages 645-655) in view of Schuurs et al (USP#4,016,043).

Harsoulis et al teaches a double antibody assay for measuring the concentration of TSH (thyroid-stimulating hormone) in urine. Urine samples were taken from subjects with well-defined clinical evidence of hypothyroidism and hyperthyroidism (see summary and introduction). The levels of TSH in the hyperthyroid subjects were lower than those of normal subjects and the level of TSH in hypothyroid subjects were higher. Claims 100 to 101 teach specific concentration ranges of TSH in urine that identify hyperthyroidism and hypothyroidism. Harsoulis et al teaches the levels of TSH was detected in concentrated normal urine (see introduction). Harsoulis et al teaches that levels in hypothyroid subjects ranged from (25·1 ± 3·3 μu./h, range 10·8-46·5μu./h) and levels in hyperthyroid subjects ranged from (2·6 ± 0·2μu./h, range , 1-3·5) and are well within the ranges taught by claims 100 and 101 (see page 652). The amount of detectable agent was bound to TSH in urine was determined utilizing a double antibody I-labeled assay (see Recovery Experiments, page 647).

Harsoulis et al does not teach the exclusion of radioimmunoassay when measuring TSH in urine.

However, Schuurs et al teaches the disadvantages of using a radioimmunoassay in that although they are sensitive, the requirement of special equipment, trained staff, the need for extra safety measures to protect against and the short half-life span of the

radioactive labeling element. The possibility of replacing the radioactive label with an enzyme label is proposed (col. 1, lines 25-42).

It would have been obvious to one of ordinary skill in the art to want to modify the teaching of Harsoulis to exclude using an radioimmunoassay and replace it with EIA as taught by Schuurs et al for extra safety measures when using radioactive products in a laboratory setting. Further, the exclusion of using radioactive products requires less disposal time, while the Enzyme Immunoassay provides a very simple, and sensitive assay method. With respect to using unconcentrated urine, one skilled in the art would be motivated to do so because it eliminates purification steps wherein the sample can be assayed upon collection, reducing the time required to perform the assay. The use of concentrated and unconcentrated urine constitute obvious variations in parameters which are routinely modified in the art and have not been described as critical to the practice of the invention.

6. Claims 110-122 and 134 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harsoulis et al, in view of Schuurs and Philo et al (USP#5,108,896).

The teaching of Harsoulis et al in view of Schuurs et al are set forth above and differ from the instant claims in not teaching dual detection of hormones.

However, Philo et al teaches a dual analyte enzyme immunoassay for assaying two antigens in a single sample wherein reactions occur simultaneously (see abstract). Philo teaches that immunoassays of the present invention are particularly advantageous for assaying pairs of antigens that are found together in physiological samples such as

human serum or urine samples. Labels utilized in the instant assay are fluorescein, rhodamine, isothiocyanate and others (col. 7, lines 12-25). Such immunoassays systems are desirable for assaying pairs of hormones including Thyroxine (T4)/ Thyroid Stimulating Hormone (TSH) and others (col. 4, lines 27-36).

It would have been obvious to one of ordinary skill in the art to modify the assay of Harsoulis et al to include measuring the concentration of Thyroxine (T4) because this hormone is found together with TSH in biological samples such as urine and blood. One skilled in the art would want to measure TSH and Thyroxine in one assay system because if TSH measurements appear discordant with clinical thyroid evaluations, Thyroxine measurements are helpful for identifying inaccurate TSH measurements. Further, dual measurements of TSH/Thyroxine can reduce the time required to run each test separately. With respect to the Thyroxine and TSH measurements of indicated hypothyroidism and hyperthyroidism, it is noted that the prior art has already established that low levels indicates hyperthyroidism while higher are indicative of hypothyroidism. Absent the evidence to the contrary, applicant's claims are directed to the same premise. The difference in units of measure are viewed as mere optimization of the prior art assays and are parameters varied in methods dependent on reagents and assays.

Response to Arguments

7. Applicant's arguments filed November 13, 2003 have been fully considered but they are not persuasive.

Applicant's argument that Examiner has not established a prima facie case of obviousness is not found persuasive. Applicant asserts that the references of Kuku et al and Shuurs et al do not teach or suggest every element of the claims. Applicant asserts that Kuku et al does not teache diagnosis of a thyroid condition in a subject and determining the concentration of TSH in the sample by a method which is not a radioimmunoassay and comparing the concentration of TSH with a urinary concentration of TSH in a normal subject in order to diagnose hypo and hyperthyroidism. Applicant asserts that Kuku et al teaches excretion rates of exogenously added I-labelled, purified human TSH in normal patients, as well as those with evidence of hypo- and hyperthyroidism by double antibody radioimmunoassay after concentration of the urine by dialysis followed by lypohilization. These arguments are noted but not found persuasive.

Although the reference of Kuku et al teaches measurement of urinary excretion rates of exogenously added intravenous pre-injection of I-labelled TSH in normal patients, one of ordinary skill in the art would do this to create a control that will distinguish between hypo and hyperthyroid patients. Once urinary TSH was measured for hypo and hyperthyroid patients, the assay concluded that urinary TSH measurement is a good discriminant between normal and hypo and hyperthyroid patients. Therefore, it is the Examiner's position that the teachings of Kuku et al teach and suggest diagnosing a thyroid conditions. Although the Applicant teaches that the instant method was not carried by radioimmunoassay, the reference of Shuurs et al teaches the

disadvantages of using a radioimmunoassay (see Office Action Paper #12, column 1, lines 25-42) and encourages other methods such as Enzyme immunoassay.

Applicant argument that the reference of Philo et al does not alone or in combination cure the deficiencies of Kuku et al and Shuurs et al because the reference do nothing but provide a general analytical method using antibodies is not found persuasive. The reference of Philo et al was relied on for its teaching of assaying analytes known to be found together in certain physiological samples which include pairs of hormones such as Thyroxine (T4) and Thyroid Stimulating Hormone (TSH) which is disclosed in the instant claims.

With respect to Applicant's argument that urinary measurement rates for TSH calculated in µU/hr taught by Kuku et al versus µIU/ml measurement rates for TSH of the instant invention cannot be properly compared have been considered and found persuasive. Therefore rejections of claims 100-101 and 121 are hereby withdrawn.

Allowable Subject Matter

8. Claims 100-101 and 121 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Conclusion

9. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah A Davis whose telephone number is (703) 308-4427. The examiner can normally be reached on 8-5 Monday thru Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deborah A. Davis
CM1, 7D16
February 3, 2004

LONG V. LE
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02/09/03